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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,861	03/08/2004	Paul Calabresi	21486-031CON2	2424

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EXAMINER

HAGHIGHATIAN, MINA

ART UNIT PAPER NUMBER

1616

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/796,861

Applicant(s)

CALABRESI ET AL.

Examiner

Mina Haghighatian

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-77 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-77 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>03/08/04</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites "A method of growth" which is indefinite. This is considered a typographical error and is interpreted as "a method of inhibiting growth" for examination purposes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 8-13, 20-26, 30-34, 45-48 and 74-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pfirrmann et al (5,593,665) in view of Morrissey et al (WO 9852572).

Pfirrmann teaches products containing tumor necrosis factor (TNF), and taurolidine and/or taurultam as a combined preparation for simultaneous, separate or sequential use for treatment of patients suffering from medical conditions mediated by TNF (see abstract). Pfirrmann discloses that the antibacterial compounds taurolidine and taurultam are significantly effective in reducing the toxicity and side effects of TNF. The findings show that taurolidine and taurultam do not inhibit the antitumour effect of TNF, but, in fact, augment such cytotoxicity. Also taurolidine and taurultam do not have significant cytotoxic effects against normal cells and may thus be safely used in combination with TNF in combating tumors (col. 1, line 58 to col. 2, line 45).

Pfirrmann teaches that other agents known to be involved in tumor metabolism may also advantageously be co-administered in conjunction with the said therapy. Such agents include gamma-interferon, interleukin-1, and interleukin-2, cytotoxic agents such as adriamycine and actinomycine (col. 2, 46-51). Pfirrmann lacks teachings on the methods of treating tumors.

Morrissey teaches the use of taurolidine for treatment of leukemia through the induction of apoptosis in leukemia cells. Taurolidine is administered by injection in solution to afflicted patients in an amount effective to cause apoptosis of monocytic

and/or myeloid cells. The cells involved in the monocytic or myeloid leukemia disease are thus attacked and die via apoptosis (page 12 lines 1-8).

Morrissey teaches the effects of taurolidine on cell viability and growth rates, where apoptosis is a controlled form of cell death characterized by the fact that neither parent cells nor apoptotic bodies become membrane-permeable. Also it was found that taurolidine causes apoptosis rather than necrosis of leukemia cells (page 22, lines 4-11).

It would have been obvious to a person of ordinary skill at the time the invention was made to have modified the teachings of Pfirrmann on the use of taurolidine and taurultam in treating tumors, by adding the method of treatments as taught by Morrissey, because of the expectations of treating patients in need of such treatments with the most effective medications and the least possible amount of side effects.

Claims 2-7, 14-19, 27-29, 35-44, 49-51 and 74-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pfirrmann et al (5,593,665) in view of Morrissey et al (WO 9852572) as applied to claims 1, 8-13, 20-24 and 45-47 above, and further in view of Samid (5,661,179).

Pfirrmann and Morrissey were discussed above. The combined references lack specific teachings on treating the various types of tumors.

Samid teaches methods for treating neoplastic conditions using phenylacetic acid and a method of treating a method of monitoring the bioavailability of a compound for

Art Unit: 1616

treatment of a pathology not associated with hemoglobin. The method comprises administering to a subject the compound and measuring the level of hemoglobin TGF-beta 2, IL-6 or TGF -alpha. Also disclosed is method of treating neoplastic condition in cells resistant to radiation and chemotherapy, specifically, the multiple drug resistant cells (col. 3, lines 34-42).

Samid teaches methods of treating malignant conditions such as prostatic cancer, melanoma, brain tumors, glioma, astrocytoma, Kaposi's sarcoma, lung adenocarcinoma, leukemia, myelodysplasia, etc (col. 7, lines 29-43).

It would have been obvious to a person of ordinary skill at the time the invention was made to have modified the combined teachings of Pfirrmann and Morrissey by substituting phenylacetate of Samid with taurolidine and/or taurultam, with a reasonable expectations of successfully producing compositions and methods of treatment for various tumors.

Claims 1-51 and 74-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monson (WO 9200743).

Monson teaches methods of treatment or prophylaxis of tumours in mammalian subjects wherein an effective dose of taurolidine and/or taurultam is administered to a mammalian subject suffering from or at risk to tumor growth (page 1, lines 18-22).

Monson discloses that taurolidine and taurultam may be administered systemically, i.e. by injection or infusion, or by direct application, e.g. topically, to

Art Unit: 1616

external tumors. Suitable formulation for injection or infusion may comprise an isotonic solution containing one or more solubilising agents in order to provide solutions of increased taurolidine or taurultam concentration (page 2, 2nd and 3rd paragraphs).

Monson teaches that other agents known to be involved in tumor metabolism may also advantageously be co-administered in conjunction with the said formulation. Such agents include interleukins, gamma-interferon, etc. Cytotoxic agents such as adriamycin and actinomycin D may be co-administered. The tumors to be treated may be of any type, including lymphomas, sarcomas, melanomas and carcinomas. It is particularly beneficial to use taurolidine and/or taurultam prevent the spread of metastases, especially following surgical removal of tumors. The mammalian subjects are typically humans (page 3, lines 1-23).

Although Monson does not specifically teach treatment or inhibition of growth of various tumors, it does disclose that taurolidine and/or taurultam may treat any type of tumor. Therefore it would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified Monson's teachings by branching off methods of treatment, prophylaxis and types of tumors.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re*

Art Unit: 1616

Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A **statutory** type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer **cannot** overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 52-73 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-22 of prior U.S. Patent No 6,429,224. This is a double patenting rejection.

Claim 77 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 20 of prior U.S. Patent No. 6,703,413. This is a double patenting rejection.

The **nonstatutory** double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 8-13, 20-26, 30-34, 45-48 and 74-76 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

Art Unit: 1616

claims 1-19 of U.S. Patent No. 6,703,413. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 8-13, 20-26, 30-34, 45-48 and 74-76 are generic to all that is recited in claims 1-19 of U.S. Patent No. 6,703,413. That is, claims 1-19 of U.S. Patent No. 6,703,413 fall entirely within the scope of claims 1, 8-13, 20-26, 30-34, 45-48 and 74-76 or, in other words, claims 1, 8-13, 20-26, 30-34, 45-48 and 74-76 are anticipated by claims 1-19 of U.S. Patent No. 6,703,413. Specifically instant claims are drawn to a method of inhibiting growth of tumor cells or a method of killing a tumor cell comprising administering a composition comprising taurolidine, taurultam or a biologically active derivative thereof. These are the same limitations set forth in claims of U.S. Patent No. 6,703,413.

Claims 1-77 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-43 of U.S. Patent No. 6,995,164. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-77 are generic to all that is recited in claims 1-43 of U.S. Patent No. 6,995,164. That is, claims 1-43 of U.S. Patent No. 6,995,164 fall entirely within the scope of claims 1-77 or, in other words, claims 1-77 are anticipated by claims 1-43 of U.S. Patent No. 6,995,164. Specifically, instant claims are drawn to a method of inhibiting growth of tumor cells or a method of killing a tumor cell comprising administering a composition comprising taurolidine, taurultam or a biologically active derivative thereof. These are the same limitations set forth in claims of U.S. Patent No. 6,995,164.

Claims 71-72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,812,251. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 71-72 are generic to all that is recited in claims 1-2 of U.S. Patent No. 6,812,251. That is, claims 1-2 of U.S. Patent No. 6,812,251 fall entirely within the scope of claims 71-72 or, in other words, claims 71-72 are anticipated by claims 1-2 of U.S. Patent No. 6,812,251. Specifically, instant claims are drawn to a method of inhibiting growth of tumor cells or a method of killing a tumor cell comprising administering a composition comprising taurolidine, taurultam or a biologically active derivative thereof. These are the same limitations set forth in claims of U.S. Patent No. 6,812,251.

Claims 1-77 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 10/980,359. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-77 are generic to all that is recited in claims 1-28 of the copending application 10/980,359. In other words claims 1-77 are anticipated by claims 1-28 of the copending application 10/980,359.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-77 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 11/350,313. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-77 are generic to all that is recited in claims 1-20 of the copending application 11/350,313. In other words claims 1-77 are anticipated by claims 1-20 of the copending application 11/350,313.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

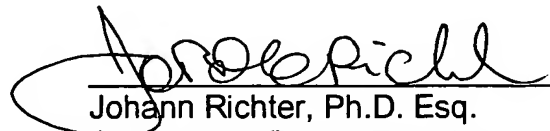
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1616

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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June 22, 2006



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